Rabies Vaccine
Biological Page

Section 7:	**Biological Product Information**		**Standard #: 07.311**
Created by:	Province-wide Immunization Program Standards and Quality		
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	Imovax® Rabies	**RabAvert®**
Manufacturer	Sanofi Pasteur SA – distributed by Sanofi Pasteur Limited	GlaxoSmithKline Inc.
Biological Classification	Inactivated	

Indications for Provincially Funded Vaccine	**Pre-exposure immunization:**
	• Rabies vaccine will be provided for the following high-risk occupational groups:
	  ○ Workers routinely caring for animals, including veterinarians, veterinary health technicians, veterinary assistants, Humane Society/SPCA workers
	  ○ Animal research workers, including rabies laboratory workers and those in other laboratories working with rabies-prone species
	  ○ Animal control workers, including bylaw officers, dog pound workers and zoo workers
	  ○ Wildlife workers, including fish and wildlife workers, foresters
	  ○ Students attending a post-secondary institution and enrolled in a veterinarian, veterinary health technician, or veterinary assistant program
	  ○ Spelunkers (cavers): Albertans involved in work-related spelunking
	Notes:
	• Volunteers, recreational spelunkers and those at risk due to international travel are not eligible to receive provincially funded rabies vaccine.
	• Employees under federal jurisdiction including the Canadian Food and Inspection Agency (CFIA) and Parks Canada are not eligible to receive provincially funded rabies vaccine.
	• Pre-exposure rabies vaccine must be ordered through Alberta Health (AH), Provincial Vaccine Depot (PVD) through your zone vaccine depot.
	• Book groups of six or more people as much as possible in order to minimize vaccine wastage. When risk of exposure is high and immediate immunization is required, consult with your zone immunization contact who will consult with Alberta Health, Immunization Program before proceeding with a vaccine series using the IM route.
	Post-exposure prophylaxis (PEP):
	• Must be considered for individuals of all ages if potential exposure to rabies virus has occurred. The animal species, the incident and the type of exposure must be considered as well as immunization status of the animal (if applicable) and presence of rabies in the area.
	• Pre-exposure rabies immunization does not eliminate the need for prompt post exposure prophylaxis (PEP) when a significant exposure occurs. It does eliminate the need for rabies immune globulin (RIG) and reduces the number of vaccine doses required for PEP.
	• Refer to Rabies Prevention and Control Manual Guidance for Public Health and Veterinary Professionals https://open.alberta.ca/publications/9781460142639 for risk assessment to determine if PEP is indicated.	

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	Notes: • The MOH/MOH designate within the AHS Zone will authorized the release of rabies immune globulin (RIG) or rabies vaccine for an individual. The Office of the Chief Medical Officer of Health (OCMOH) is available for consultation if desired by the MOH. • Each zone has been provided with a stock supply of RIG and rabies vaccine from AH PVD to initiate post exposure prophylaxis. • Follow-up of individuals from out of province requiring rabies PEP should be discussed with zone MOH/MOH designate and referred directly to AH Immunization Program. The AH Nurse Consultant will send a referral to the appropriate jurisdiction to ensure follow up is completed.	
Serology	**Pre-exposure:**	
	Primary series: • Rapid fluorescent-focus inhibition test result of less than 0.5 IU/mL indicates the need for a reinforcing dose. • Due to inherent imprecision in the rabies assay (RFFIT), individuals with test results reported as 0.5 IU/mL up to and including 1.0 IU/mL who are at increased or continuing risk of rabies exposure should be offered a reinforcing dose of rabies vaccine. • When ID administration of the vaccine is used, serology should be done at least 2 weeks after the third dose to ensure adequate protection. If protection is not adequate a reinforcing dose using the ID route should be offered. Following the reinforcing dose serology should be repeated at least 2 weeks after this reinforcing dose. Consult with zone MOH/MOH designate if adequate protection is still not achieved. • Serology is recommended 7 to 14 days after pre-exposure immunization in immunocompromised individuals (due to illness or immunosuppressive agents), or those taking chloroquine or hydroxychloroquine. If an acceptable response is not achieved a second series of vaccine should be administered followed by serological testing.	
	Reinforcing doses: • Antibody determination should precede any reinforcing dose of vaccine. Rapid fluorescent-focus inhibition test result of less than 0.5 IU/mL indicates the need for a booster dose. • Individuals with test results reported as 0.5 IU/mL up to and including 1.0 IU/mL who are at increased or continuing risk of rabies exposure should be offered a reinforcing dose of rabies vaccine. • Determination of immunity is recommended every 2 years for individuals at continuing risk (occupational groups listed under indications) of rabies exposure. • Research lab workers working with live rabies virus at risk of unapparent exposure should be tested for rabies immunity every 6 months. • When ID administration of the vaccine is used, serology should be done at least 2 weeks after the reinforcing dose to ensure adequate protection. Consult with zone MOH/MOH designate if adequate protection is not achieved.	
	Post-exposure prophylaxis:	
	• Serology is recommended 7 to 14 days after post-exposure immunization in immunocompromised individuals (due to illness or immunosuppressive agents), or those who are taking chloroquine or hydroxychloroquine. If an acceptable response is not achieved a second series of vaccine should be administered followed by serological testing. • Serology may be recommend by the MOH if a dose in the routine post-exposure prophylaxis schedule is missed. **Serology requisition** is located on the Alberta Health Services external webpage under Laboratory Services – Provincial Laboratory for Public Health (ProvLab)	

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	http://www.albertahealthservices.ca/lab/Page3320.aspx - use Zoonotic Serology Requisition.	

Schedule	**Pre-exposure:**
	Primary series (3 doses):
	• Dose 1 – day 0
	• Dose 2 – day 7
	• Dose 3 – day 21 to 28
	Reinforcing doses:
	• It is recommended that the following individuals receive reinforcing doses of vaccine based on determination of immunity and ongoing risk of exposure. See Serology Section for recommendations.
	  ○ Every 6 months for research lab workers working with live rabies virus at risk of unapparent exposure
	  ○ Every 2 years for individuals with continuing risk (occupational risk groups listed above).
	  ○ Antibody determination should precede any reinforcing dose of vaccine.
	Notes:
	• When ID administration of the vaccine is used, serology should be checked at least two weeks after completion of the vaccine series or after a reinforcing dose to ensure adequate protection.
	• Immunocompromised individuals should have serology 7 to 14 days post-immunization to ensure an acceptable antibody concentration has been achieved. If an acceptable response is not obtained, a second series of vaccine should be administered followed by serologic testing.
	• Individuals who have received an undocumented rabies series and present-with rabies serology indicating inadequate immunity should be offered a reinforcing dose. Serology should be checked at least two weeks after the reinforcing dose. If serology following the reinforcing dose indicates inadequate immunity, offer two more doses to complete a series.	

	Post-exposure prophylaxis:
	Previously **unimmunized** individuals who are:
	Immunocompetent: <u>4 doses</u>
	• **IM –** 1.0 mL each
	<u>OR</u>
	• **ID** - 0.1 mL each at two anatomical sites (for a total of 0.2 mL)
	  ○ Dose 1 – day 0 (day 0 is the day the first dose is administered)
	  ○ Dose 2 – day 3
	  ○ Dose 3 – day 7
	  ○ Dose 4 – day 14
	Notes:
	  ○ ID administration is the preferred route of administration (unless contraindicated) when operationally feasible and clients can be clustered.
	  ○ Series may be completed using a mixed IM/ID schedule as long as the scheduling is maintained.
	Immunocompromised individuals (due to illness or immunosuppressive agents), or those who are taking chloroquine or hydroxychloroquine: **<u>5 doses</u>**
	• **IM –** 1.0 mL each
	  ○ Dose 1 – day 0 (day 0 is the day the first dose is administered)
	  ○ Dose 2 – day 3
	  ○ Dose 3 – day 7
	  ○ Dose 4 – day 14
	  ○ Dose 5 – day 28	

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	Note: • Rabies Immune Globulin (RIG) should be administered to previously unimmunized individuals on day 0 at the same time as dose 1 of rabies vaccine but at a different anatomical site from the vaccine. Previously **appropriately immunized** individuals: **2 doses** • **IM –** 1.0 mL each **OR** • **ID** - 0.1 mL each at two anatomical sites (for a total of 0.2 mL) Unless immunocompromised or taking chloroquine or hydroxychloroquine ○ Dose 1 – day 0 ○ Dose 2 – day 3 ○ RIG should **not** be administered for persons who are appropriately immunized (see notes below for further details). **Note:** If the individual is immunocompromised or taking chloroquine or hydroxychloroquine 1.0 mL rabies vaccine IM should be administered. **Notes:** **Appropriate rabies immunization consists of:** • Documentation of a complete series of pre or post exposure immunization with human diploid cell vaccine (HDCV) as in Imovax® Rabies or purified chick embryo cell vaccine (PCECV) as in RabAvert®. • Documentation of complete immunization series with: ○ other types of rabies vaccine OR ○ HDCV or PCECV according to unapproved schedules OR ○ ID rabies series with HDCV or PCECV vaccine AND ○ Serology demonstrating an antibody response (0.5 IU/mL or greater) following completion of the immunization series. • If vaccine other than HDCV or PCECV was used for pre-exposure immunization and the person's immune status is not known, a full course of treatment, including RIG, should be initiated. A serum sample may be collected before the vaccine is administered, and if adequate protection is demonstrated, the vaccine series may be discontinued, provided at least two doses of vaccine have been administered. **Recommendations for post-exposure series initiated in another country:** • If the post-exposure series initiated meets the World Health Organization (WHO) approved vaccines, and meets WHO approved schedule - complete the series as appropriate. • WHO approved vaccines include cell culture vaccines (purified chicken embryo vaccine, purified Vero cell rabies vaccine and human diploid cell vaccine) and duck embryo vaccine. • See attached links for additional information: ○ WHO Expert Consultation on Rabies https://apps.who.int/iris/bitstream/handle/10665/272364/9789241210218-eng.pdf ○ CATMAT Rabies Statement: http://www.phac-aspc.gc.ca/tmp-pmv/catmat-ccmtmv/index-eng.php • RIG can be offered if the client has not already received RIG and it can be administered within seven days of the first dose of rabies vaccine. • For uncertain vaccines or unknown schedules, including no clear documentation - restart series and offer RIG. **General Notes related to post-exposure prophylaxis:** • **Rabies post-exposure vaccine schedules should be adhered to as closely as possible and it is essential that all recommended doses of vaccine be administered.** ○ It is critical that the **first 3 doses** be spaced according to the schedule.	

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	○ Prolonging the interval between doses may seriously delay achieving the protective antibody titres, with potentially fatal consequences. ○ If a dose in the routine post-exposure prophylaxis schedule is missed, consult the MOH. Series should be resumed as soon as possible respecting the minimum intervals between doses. See Section 5 of the Standard for Recommended Immunization Schedules. • If RIG is not administered at the initiation of the rabies vaccine series (day 0), it can be administered up to and including day 7 after the first dose of rabies vaccine. • Immunocompromised individuals (due to illness or immunosuppressive agents) or those taking chloroquine or hydroxychloroquine, should have a rabies antibody determination following completion of PEP to ensure that an acceptable level has been achieved. • If an individual needs to complete the post-exposure series outside of Alberta, contact Alberta Health Immunization Program for assistance in making the arrangements to complete the vaccine series.	
Preferred Use	There is no preference indicated for the use of Imovax® Rabies or RabAvert® in specific age or risk groups. • Both vaccines are safe and immunogenic in all individuals. • Individuals with medical contraindications to one product should be offered the alternate product if supply is available.	
Dose	**Pre-exposure:** • 0.1 mL if given by the Intradermal (ID) route OR • 1.0 mL if given by the Intramuscular (IM) route if ID administration is contraindicated **Post-exposure:** • 0.1 mL ID each at two anatomical sites (for a total of 0.2 mL) OR • 1.0 mL given by the IM route (if ID administration is contraindicated or not operationally feasible)	
Route	**Pre-exposure:** **ID or IM if the ID route is contraindicated:** • **ID** injection (deltoid site), unless contraindicated is the preferred route for healthy individuals for the primary series and reinforcing doses. **Note:** ○ After reconstitution, the vaccine must be used as soon as possible and within 6 hours ○ Although rabies vaccine is not specifically licensed in Canada for ID administration, the World Health Organization (WHO) considers the ID regimen an acceptable alternative to IM administration as it uses less vaccine to produce a comparable degree of protection against rabies. Several Canadian provinces also provide pre-exposure rabies vaccine using the ID route for administration. • **IM** injection must be used for individuals who are immunocompromised due to illness or immunosuppressive agents, or those individuals who are taking chloroquine or hydroxychloroquine. The immune response to receiving vaccine ID may not be protective under these circumstances. Therefore for these individuals, the vaccine should be administered by the IM route only. ○ The gluteal region should never be used for IM administration of rabies vaccine because administration in this area can result in a lower antibody response. ○ The deltoid area is the preferred site for adults and older children. For infants and younger children use the vastus lateralis.	

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	Post-exposure:
	ID or IM injection if ID is contraindicated or not operationally feasible:
	• **ID** injection (deltoid site)
	  ○ When administering the rabies vaccine by the ID route, a bleb must be present; if not a repeat dose at a site a minimum of 1 inch away from the previous injection site is required.
	  ○ After reconstitution, the vaccine must be used as soon as possible and within 6 hours.
	• **IM** injection must be used for individuals who are immunocompromised due to illness or immunosuppressive agents, or those individuals who are taking chloroquine or hydroxychloroquine. The immune response to receiving vaccine ID may not be protective under these circumstances. Therefore for these individuals, the vaccine should be administered by the IM route only.
	  ○ The gluteal region should never be used for IM administration of rabies vaccine because administration in this area can result in a lower antibody response.
	  ○ The deltoid area is the preferred site for post-exposure immunization of adults and older children. For infants and younger children use the vastus lateralis.	

Contraindications/ Precautions	**Contraindications:**
	• **Pre-exposure:**
	  ○ Known severe hypersensitivity to any of the components of the vaccine or the vaccine container.
	  ○ Anaphylaxis or other severe allergic reaction to a previous dose of vaccine containing rabies antigen.
	• **Post-exposure:**
	  ○ Because rabies disease is almost always fatal, there is no contraindication to rabies PEP. However, consultation with the MOH should occur for the management of individuals who are hypersensitive to the vaccine or any ingredients in the formulation or the vaccine container.
	Precautions:
	• Individuals with a history of severe hypersensitivity reactions to egg or egg products should be given an HDCV vaccine such as Imovax® Rabies and should not receive RabAvert®.
	• Immunocompromised individuals may have a suboptimal response to rabies vaccine.
	• Immune suppressive agents or chloroquine and hydroxychloroquine should not be administered during post-exposure prophylaxis unless essential for the treatment of other conditions. Consult with your zone MOH on a case by case basis when providing post-exposure prophylaxis to immunocompromised clients.	

Possible Reactions	**Common:** • Pain, erythema, induration, bruising and itching at the injection site • Headache, nausea, abdominal pain, vomiting, diarrhea, decreased appetite, asthenia, muscle aches, arthralgia, malaise, fever, chills, adenopathy, rash and dizziness **Note:** • Systemic allergic reactions characterized by generalized urticaria and accompanied in some cases by arthralgia, angioedema, fever, nausea and vomiting have been reported. These reactions are uncommon in people receiving primary immunization but have occurred in up to 7% of those receiving a booster dose, with an onset after 1 to 21 days. **Rare:** • Anaphylaxis • Paresthesia, hyperhidrosis (sweating) • As with any immunization, unexpected or unusual side effects can occur. Refer to the product monograph for more detailed information.	

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Pregnancy	• Pregnancy is not a contraindication to post-exposure rabies immunization. • If there is a substantial risk of exposure to rabies, pre-exposure immunization may be indicated during pregnancy.	
Lactation	• Breastfeeding is not a contraindication to rabies immunization. • It is not known whether rabies vaccine or corresponding antibodies cross into breast milk.	
Composition	Each 1.0 mL dose of reconstituted vaccine contains: • 2.5 IU or more of rabies antigen • Less than 100 mg Human albumin • Less than 150 mcg Neomycin • 20 mcg phenol red indicator • Sterile water for injection (diluent) Contains no preservative or stabilizer	Each 1.0 mL of reconstituted vaccine contains: • 2.5 IU or more of rabies antigen • Less than 12 mg polygeline (processed bovine gelatin) • Less than 0.3 mg human serum albumin • 1 mg potassium L-glutamate • 0.3 mg disodium edetate) • Less than 3 ng ovalbumin (chicken protein) • Less than 10 mcg neomycin • Less than 200 ng chlortetracycline • Less than 20 ng amphotericin B • Traces of bovine serum • Sterile water (diluent) Contains no preservative
Blood/Blood Products	Each 1.0 mL dose of reconstituted vaccine contains less than 100 mg human albumin.	Each 1.0 mL dose of reconstituted vaccine contains less than 0.3 mg human serum albumin.
Bovine/Porcine Products	• Bovine-derived products may be present in small amounts either as components of the culture media used to manufacture or as a component of the final product. • Porcine-derived products are used as raw materials in the early stages of the manufacturing process.	• Contains less than 12 mg polygeline (processed bovine gelatin). • Small quantities of bovine serum used in cell culture process. • No mention of porcine products used in the manufacturing process.
Latex	There is no latex in the vaccine or vaccine packaging.	
Interchangeability	The immunization series should be, whenever possible, completed with the same product. However, if this is not possible, RabAvert® and Imovax® Rabies are considered interchangeable in terms of indications for use, immunogenicity, efficacy and safety.	
Administration with Other Products	• Imovax® Rabies/RabAvert® vaccine and RIG should be administered concurrently when indicated for rabies (PEP) using separate needles/syringes and different anatomical sites. • Inactivated vaccines and live vaccines may be given at the same time using separate needles/syringes and different injection sites. • Chloroquine and hydroxychloroquine and immunosuppressive agents may diminish the protective efficacy of the vaccine.	
Appearance	Freeze-dried vaccine is pinkish beige to orangey yellow. The diluent is a clear, colourless liquid. After reconstitution, the vaccine is clear or slightly opalescent red to purplish red suspension.	The white freeze-dried vaccine when reconstituted with the sterile water diluent dissolves to a clear to slightly opalescent, colourless to slightly pink solution.
Storage	• Store at +2°C to +8°C • Do not freeze • Do not use beyond the labeled expiry date	

	• Store in original packaging when possible to protect from light • Reconstituted vaccine should be used as soon as possible and within 6 hours	
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Vaccine Code	RAB	
Antigen Code	RAB	
Licensed Use	Pre-exposure and Post-exposure: • 1.0 mL administered by intramuscular route to all eligible individuals.	
Off-License Use	Pre-exposure: • 0.1 mL administered by intradermal route to eligible individuals. Post-exposure: • 0.1 mL administered by intradermal route to two anatomical sites to eligible individuals (for a total of 0.2 mL).	

Program Notes:

- 1980 January 1: Rabies vaccine was introduced into program.
- 1999 August: Imovax® Rabies vaccine introduced.
- 2005 June 1: RabAvert® Rabies vaccine introduced.
- 2013 August 29: Schedule change for Rabies PEP - introduced a 4 dose (versus 5 dose) post-exposure vaccine immunization schedule for immune competent individuals.
- 2016 November 16: Recommendations included for post exposure series initiated in another country.
- 2019 October: Alternate route and dose of post-exposure rabies vaccine. Vaccine to be administered ID (2 site 0.1 mL) when operationally feasible with the exception of immunocompromised individuals.
- 2022 February 28: Clarified recommendation for individuals being assessed for pre-exposure rabies vaccine reporting undocumented rabies immunization series.

Related Resources:

- Rabies Vaccine Information Sheet
- RabAvert® Vaccine Instructions for Reconsititution https://www.drugs.com/dosage/rabavert.html

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